A CLINICOPATHOLOGICAL STUDY OF MICRONODULAR AND MACRONODULAR CIRRHOSIS IN BELFAST, NORTHERN IRELAND

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THE definition of cirrhosis is essentially anatomical, with an additional clinical concept. This is based on the "Report of the Board for Classification and Nomenclature of Cirrhosis of the Liver" at the Fifth Pan-American Congress of Gastroenterology in Cuba (Gastroenterology 1956). The cases of cirrhosis in the present study conformed to the criteria laid down at this Congress. The pathological classification of cirrhosis is unsatisfactory and various synonyms have been used to describe the same lesion. Broadly, cirrhosis may be classified anatomically as micronodular or macronodular in type. The micronodular type has been variously named portal, nutritional, fine or Laennec's cirrhosis. The features of micronodular or portal cirrhosis were those described by Baggenstoss and Stauffer (1952). The macronodular type of cirrhosis has also been termed coarsely nodular cirrhosis, postnecrotic or posthepatitic in type. Popper (1966) has distinguished two subcategories of macronodular cirrhosis—postnecrotic and posthepatitic (Gall, 1960).

The different anatomical types of cirrhosis are probably points along a continuum and not separate entities. In the later stages of the disease the distinctive features of most aetiological types of cirrhosis tend to disappear, and the end-stage liver is usually coarsely fibrotic, shrunken and macronodular. In the present study, macronodular (postnecrotic and posthepatitic) cirrhosis was diagnosed from both the gross and microscopic appearances as described by Baggenstoss and Stauffer (1952), Steiner (1960) and Gall (1960). Macronodular cirrhosis was not subdivided into two subcategories in the present study. The livers in this study represented mostly the end-stage with a micronodular or macronodular cirrhosis pattern. The incidence of liver cirrhosis was determined and a comparative pathological study of micronodular and macronodular cirrhosis made in Belfast, Northern Ireland.

MATERIALS AND METHODS

Cases of cirrhosis of the liver including micronodular (portal) and macronodular (postnecrotic/posthepatitic) cirrhosis were selected from autopsies performed at the Royal Victoria Hospital, Mater Infirmorum and City Hospitals, Belfast, from January 1, 1938 to December 31, 1966 inclusive. The clinical records were reviewed, and all histological material was re-examined. The sections were stained with haemtoxylin and eosin (H & E) and Perls' reaction for haemosiderin.

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Results

During the years 1938 to 1966 inclusive, 22,050 autopsies were performed. According to the criteria postulated earlier, there were 170 cases of micronodular cirrhosis and 168 cases of macronodular cirrhosis.

Micronodular (Portal) cirrhosis: There were 170 cases in which the morphological and histological data suggested micronodular cirrhosis. The youngest patient was 27 yr. of age and the oldest 97 yr.; the average age was 62 yr. There were 87 males and 83 females with an average age of 60 and 64 respectively.

Macronodular (Postnecrotic/Posthepatitic) cirrhosis: There were 168 cases, of whom 89 were males and 79 females. The youngest was aged 4 yr. and the oldest 87 yr. The average age was 58 yr., and there was no appreciable difference in the age between males and females. Eight cases (4.7 per cent) were under 20 yr. of age. The incidence, sex distribtuion and ages in these groups of cases with liver cirrhosis are shown in Table I.

TABLE I

Incidence, sex distribution and ages in micronodular (portal) cirrhosis and macronodular (postnecrotic/posthepatitic) cirrhosis in 22,050 autopsies.

Observations	*Type of cirrhosis*	
	Micronodular	*Macronodular*
Number of cases	170	168
Incidence relative to 100,000 autopsies	770	761
Distribution Male : Female	1 : 1 (87 : 83)	1.1 : 1.0 (89 : 79)
Average age (in years)	62	58
Range (in years)	27–97	4–87
Number <20 years	0	8 (4.7 per cent)

Incidence of liver cirrhosis

The frequency with which liver cirrhosis is found at autopsy varies from series to series. These figures probably depend on available hospital facilities, the frequency of autopsy and whether there is a particular interest in liver diseases. In this series, there are 640 cases of liver cirrhosis, of which 170 were micronodular cirrhosis, 168 macronodular cirrhosis, 140 biliary cirrhosis, 121 cardiac cirrhosis, and 40 cases that were not classified. Thus the incidence of liver cirrhosis was found to be 2.9 per cent of all autopsies preformed during 1938 to 1966 inclusive. The incidence of liver cirrhosis found at autopsy in different countries is shown in Table II, adapted from Hällén and Krook's (1963) paper on liver cirrhosis. The incidence of liver cirrhosis in European countries varies from 1.8 to 3.3 per cent, but a higher incidence seems to be present in the United States of America. A very high incidence is present in Chile, but the number of

TABLE II

Incidence of liver cirrhosis found at autopsy in different countries (Adapted from Hällén and Krook 1963)

Country	*Authors*	*No. of autopsies*	*Cirrhosis (%)*
Austria	Holtzner et al (1956)	24,008	1.8
Chile	Armas-Cruz et al (1951)	400	8.5
Germany	Langer, Honus (1954)	40,126	2.5
U.S.A.	Hall et al (1953)	16,600	4.4
U.S.A.	Kirshbaum, Shure (1943)	12,267	2.8
Sweden	Hällén, Krook (1963)	8,279	3.3
N. Ireland	Present Study (1972)	22,050	2.9

autopsies performed is small, and there may have been selection of cases for autopsy, giving a high incidence of liver cirrhosis.

Clinical data prior to final admission

The clinical notes of cases with micronodular cirrhosis and macronodular cirrhosis were consulted, but as some of the case records were insufficient with respect to certain clinical data, this aspect of the study may be subject to error. The main clinical findings are shown in Table III.

TABLE III

Clinical Data Prior to Final Admission.

Observations	*Types of Cirrhosis*					
	Micronodular (170 cases)		*Macronodular (168 cases)*		*Extrahepatic Disease 500 cases*	
	No. of cases	*Per cent.*	*No. of cases*	*Per cent.*	*No. of cases*	*Per cent*
Syphilis (+ve W.R.)	20	11.7	8	4.7	6	1.2
Excess alcohol intake	34	20.0	20	11.9		
Diabetes mellitus	20	11.7	5	2.9	13	2.6
History of jaundice or "hepatitis"	6	3.5	24	14.2		
No. diagnosed before autopsy	69	40.4	114	68.0		

Syphilis or a positive Wassermann test had been noted in 11.7 per cent of patients with micronodular cirrhosis, and 4.7 per cent with macronodular cirrhosis. Syphilis was recorded in 1.2 per cent of the autopsies performed in this institute. In none of the cases was the disease regarded as active or as being per se of aetiological importance in liver cirrhosis.

A statement concerning excess intake of alcohol was made in the clinical records of 20 per cent of the patients with micronodular cirrhosis and in 11.9 per cent with macronodular cirrhosis. The alcohol consumed was mainly beer or whisky. Jolliffee and Jellinek (1941) stated that the incidence of cirrhosis in alcoholics was 6.8 times more in inebriates than in the general population. It has been suggested that the cirrhosis is nutritional in alcoholics, as they tend to have a low protein intake, especially choline deficiency, but the cirrhosis has not been clearly established as nutritional.

Diabetes mellitus occurred in 2.9 per cent of cases with macronodular cirrhosis, and in 11.7 per cent with micronodular cirrhosis. Only 2.6 per cent of the patients autopsied in this institute had a clinical diagnosis of diabetes mellitus. Hällén and Krook (1963) found diabetes in 13.0 per cent of their cases of liver cirrhosis, as compared with 5.8 per cent in patients autopsied at their centre during 1957 to 1960. MacDonald (1964) also found that diabetes mellitus was more common in patients with portal cirrhosis than in those without cirrhosis.

Number of patients diagnosed before autopsy

Sixty-eight per cent of patients with macronodular cirrhosis and 40.4 per cent with micronodular cirrhosis were diagnosed before death to have liver cirrhosis. The higher rate of diagnosis was made in patients with macronodular cirrhosis due no doubt to the greater degree of hepatocellular damage than is found in cases with micronodular cirrhosis.

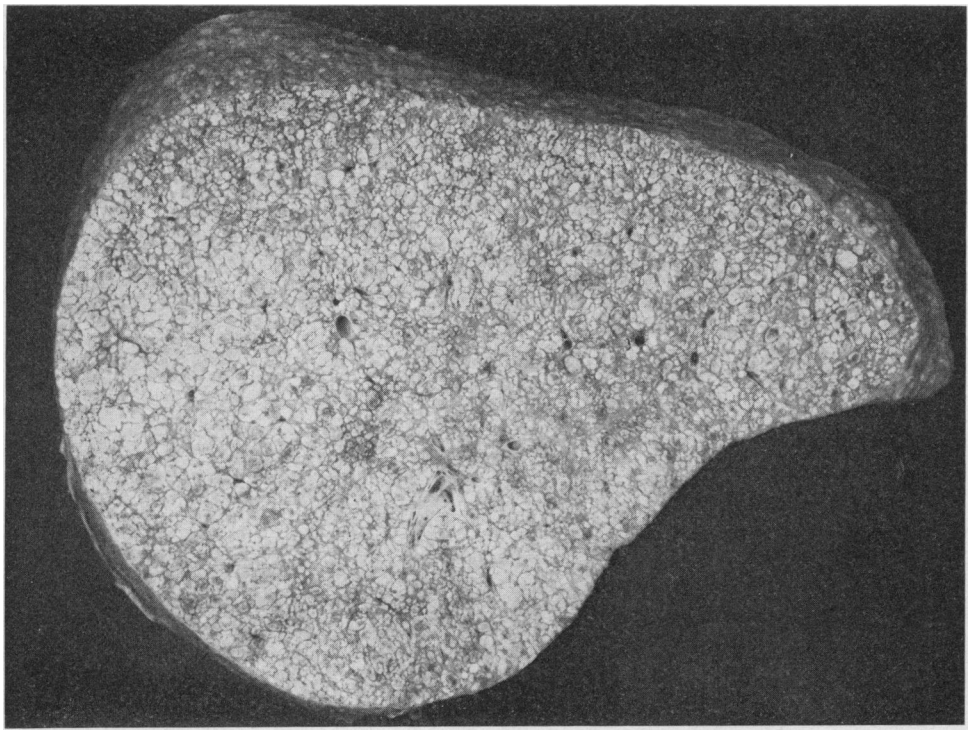
PATHOLOGICAL ASPECTS

Hepatic lesions in micronodular (portal) cirrhosis

The livers weighed between 540g and 3360g, the average weight being 1730g. In 46 per cent (78) of cases, the livers weighed over 1500g, assuming 1500g as the weight of a normal liver. The livers were granular and the regenerative nodules varied in size, but were generally smaller than 5 mm. in diameter. The typical macroscopic appearance of a liver showing micronodular cirrhosis is seen in Fig. 1. In 29.5 per cent of cases infiltration with fat was mild, and moderate to severe in 15 per cent. There was no fat infiltration in 55.5 per cent. There was mild infiltration by lymphocytes in 65.3 per cent (111 cases) and moderate to severe infiltration in 21.2 per cent (36). There was slight bile duct proliferation in 60 per cent (102), and moderate to severe in 7 per cent (12) of the livers. The fibrous bands were narrow and the internodular connective tissue caused extensive distortion of both hepatic and portal venules. These features are shown in Fig. 2.

Hepatic lesions in macronodular (postnecrotic/posthepatitic) cirrhosis

The weight of the livers ranged from 550g to 3500g, with an average weight of 1300g. Thirty-two per cent (54) weighed more than 1500g. The livers were nodular, and the nodules varied from 5 mm. to 2 cm. in size. The bands of fibrous tissue separating the regenerating nodules were thicker than in the livers of micronodular cirrhosis, and the nodules were of varying sizes as shown in Fig. 3. Infiltration with fat was mild in 19 per cent (32) and moderate to severe in 6.5 per cent (11)



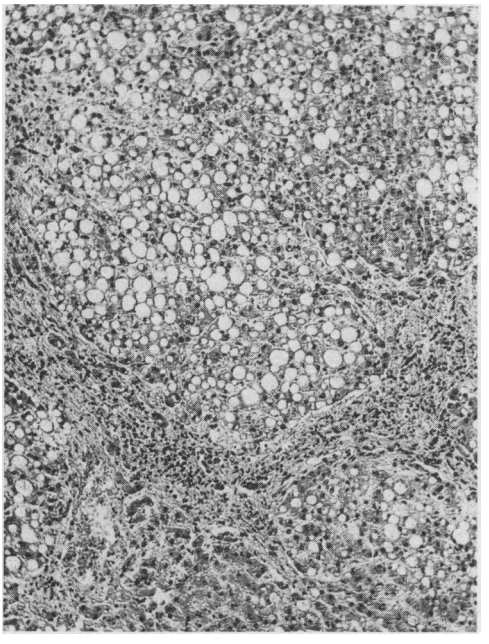


FIG. 1. *Section of liver showing a fine diffuse nodularity as seen in micronodular or portal cirrhosis. The nodules vary in size but are less than 5 mm. in diameter.*

FIG. 2. *Microscopic appearance of micronodular (portal) cirrhosis. There is fatty change and some liver cells are necrotic. Fine fibrous bands dissect the liver. There is lymphocytic infiltration with bile duct proliferation in the fibrous bands* (H. & E. x 110).

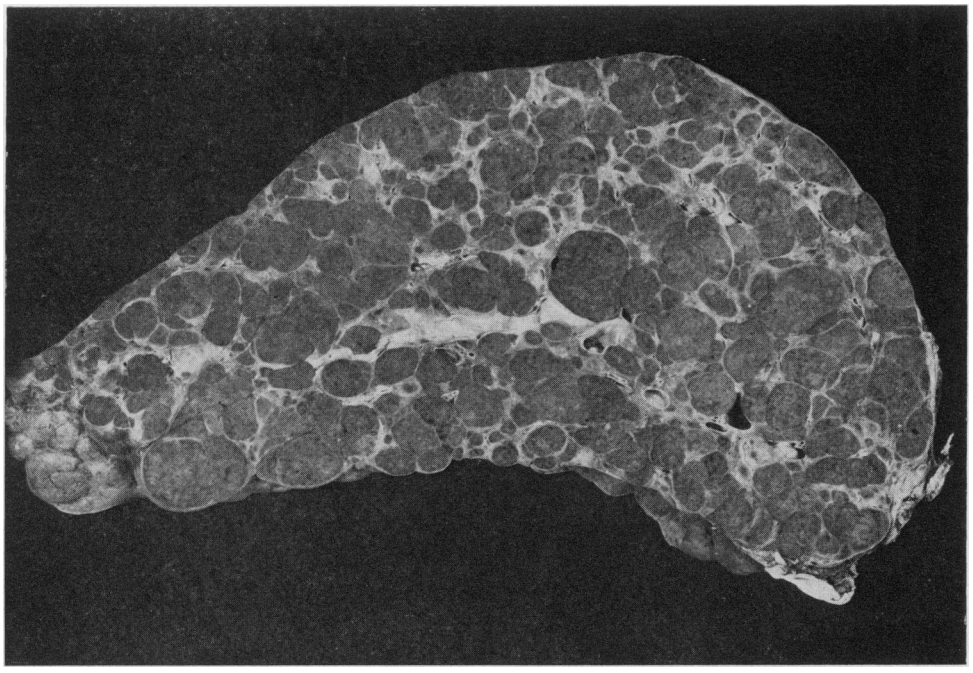


FIG. 3. *Section of the liver showing a coarsely nodular pattern as seen in macronodular cirrhosis. The regenerating nodules measure 5 mm. to 2 cm. or more in diameter and are separated by broad bands of fibrous tissue.*

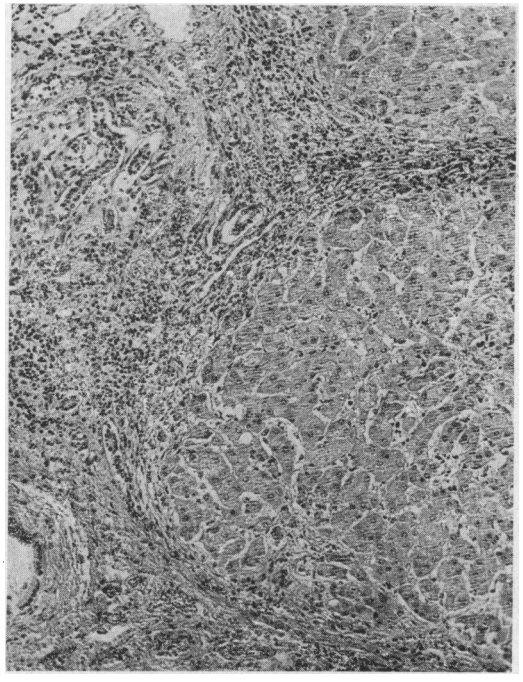


FIG. 4. *Microscopic appearance of macronodular (postnecrotic) cirrhosis of the liver. Broad bands of fibrous tissue containing proliferating bile ducts and lymphocytes, intersect nodules of regenerating liver cells which are larger than in portal cirrhosis. There is no fatty change* (H. & E. x 110).

of cases. There was no fat infiltration in approximately 75 per cent. There was moderate to severe bile duct proliferation in 67.2 per cent (113) and mild proliferation in 13.6 per cent (23) of the cases. There was moderate to severe infiltration by lympocytes and mononuclear cells in about 81.5 per cent (135) of the livers examined. In others there was mild leucocytic infiltration. The histological features are shown in Fig. 4. A summary of the macroscopic and histological features in micrnodular cirrhosis and macronodular cirrhosis is shown in Tables IV and V.

TABLE IV

Findings at autopsy in micronodular cirrhosis and macronodular cirrhosis

Observations	*Type of cirrhosis*			
	Micronodular (170 *cases*)		*Macronodular* (168 *cases*)	
	No. of cases	*Per cent*	*No. of cases*	*Per cent*
Average weight of liver	1730g		1330g	
Liver > 1500g	78	46.0	54	32.0
Average weight of spleen	335g		415g	
Spleen > 250g	83	49.0	117	70.0
Ascites	47	27.6	91	54.1
Oesophageal varices	38	22.3	88	52.3
Rupture of	26	*(68.4)	55	*(62.5)
Peptic ulcer	26	15.2	11	6.5
Primary hepatic carcinoma				
Total	12	7.0	37	22.0
Type: Hepatocellular	11 (9 R. lobe)	**91.6	32 (12 R. lobe)	**86.5
Cholangiocarcinoma	1	** 8.4	4	**10.8
Mixed	0	** —	1	** 2.7
Portal vein thrombosis				
Total	2	1.1	12	7.1
No. associated with liver carcinoma	1	***(50)	10	***(83.3)

*Expressed as a percentage of the total number of oesophageal varices.
**Expressed as a percentage of the total number of cases with primary hepatic carcinoma.
***Expressed as a percentage of the total number of cases with portal vein thrombosis.

TABLE V

Histological features in micronodular (portal) cirrhosis and macronodular (postnecrotic/posthepatitc) cirrhosis.

Observations	*Type of cirrhosis*	
	Micronodular (170 *cases*)	*Macronodular* (168 *cases*)
Morphological appearances	Altered uniformly	Altered: large areas of atrophy
Regenerative nodules	Uniform size < 5 mm.	Greater variations in size > 1 cm.
Infiltration with fat	Moderate to severe 15 per cent	Moderate 6.5 per cent
	Mild 29.5 per cent	Mild 19 per cent
Internodular fibrous tissue	Narrow zones	Wide zones
Bile ducts	Mild to moderate proliferation	Moderate to marked proliferation
Leucocytes	Mild to moderate lymphocytosis	Moderate to marked lymphocytosis

Other findings at autopsy

Evidence of portal hypertension

Splenomegaly (weight above 250g) was present in 70 per cent of patients with macronodular cirrhosis, and in 49 per cent with micronodular cirrhosis. Oesophageal varices were demonstrated in 52.3 per cent of cases with macronodular cirrhosis and in 22.3 per cent with micronodular cirrhosis. Ascites was found in 54.1 per cent of patients with macronodular cirrhosis and in 27.6 per cent with portal cirrhosis. Thus portal hypertension as evidenced by splenomegaly, oesophageal varices and ascites was observed more frequently in macronodular cirrhosis than in micronodular cirrhosis. Sixty to 68.4 per cent of the varices bled in both groups.

Peptic ulcer

This was found in 3.7 per cent of autopsies performed in this institute. Peptic ulceration was observed in 6.5 per cent of cases with macronodular cirrhosis and in 15.2 per cent with micronodular cirrhosis. MacDonald (1964) found that 14 per cent of patients with portal cirrhosis had peptic ulcer. Hällén and Krook (1963) found that 11 per cent of their cases with liver cirrhosis had peptic ulcer. The increased incidence of peptic ulcer in portal or micronodular cirrhosis may be due to the more frequent alcohol intake in these cases causing gastric irritation and faulty nutrition. It has been suggested that in liver cirrhosis there is an increased level of circulating plasma histamine, due to decreased breakdown by the liver cells, and it is this increased circulating level of histamine which causes peptic ulcer by increasing gastric acidity; but the exact mechanism is still obscure.

Primary hepatic carcinoma

This tumour was observed in 7 per cent of the patients with micronodular cirrhosis and in 22 per cent with macronodular cirrhosis. Hepatocellular carcinoma was the most common type (91 per cent), and cholangiocarcinoma was found in 9 per cent (5) of the 54 cases with a primary carcinoma of the liver. The right lobe of the liver was the commonest site for the development of the tumour in micronodular cirrhosis. In macronodular cirrhosis, 54 per cent of the tumours had a diffuse or multicentric origin. Hällén and Krook (1963) observed primary carcinoma of the liver in 11 per cent of autopsy series on liver cirrhosis. They found an equal frequency of carcinoma of the liver in the two aetiological groups studied by them—"alcoholic" and "posthepatitic" cirrhosis. The increased frequency of primary carcinoma of the liver in macronodular cirrhosis is explained by MacDonald (1964) on the basis that these patients represent an end stage of portal cirrhosis; "they have had cirrhosis for a number of years, with a long interval between early liver injury and the development of carcinoma."

Portal vein thrombosis

The incidence of portal vein thrombosis in macronodular cirrhosis was 7.1 per cent, and in the majority (81 per cent) of these patients there was an associated primary liver cell carcinoma. Approximately 1 per cent of patients with micronodular cirrhosis had portal vein thrombosis.

The Pancreas

Twenty per cent of autopsies with extrahepatic disease showed interacinar and inter-lobular pancreatic fibrosis, with minimal lymphocytic or adipose infiltration. Loss of cells in the islets was seen in 7 per cent, and hyalinization in 2 per cent of the control autopsies. No diabetes mellitus was recorded in these cases.

In micronodular (portal) cirrhosis 44.7 per cent of the 170 patients showed some degree of pancreatic fibrosis with atrophy of the acini. In 14 per cent of the cases, there was a mild to moderate leucocytic infiltration, mainly lymphocytic. In six patients, the islets of Langerhans were hyalinized and four of these cases had diabetes mellitus. There was poor cellularity of the islets in 29 patients, of whom six had diabetes mellitus.

In macronodular (postnecrotic/posthepatitic) cirrhosis pancreatic fibrosis with atrophy of the acinar glands was seen in 53 per cent of the 159 patients examined. There was lymphocytic infiltration of the fibrous tissue in 9.4 per cent of the cases. The islets of Langerhans were hyalinized in six cases, and two of these patients had diabetes mellitus. A summary of the findings in the pancreas in the autopsied patients with extrahepatic disease, and micronodular and macronodular cirrhosis is shown in Table VI.

TABLE VI

Findings in the pancreas in control autopsies with extrahepatic disease, micronodular cirrhosis and macronodular cirrhosis.

Observations	*Types of cases*					
	Controls (100 *cases*)		*Micronodular cirrhosis* (170 *cases*)		*Macronodular cirrhosis* (159 *cases*)	
	No. of cases	*Per cent*	*No. of cases*	*Per cent*	*No. of cases*	*Per cent*
Pancreatic fibrosis	20	20	76	44.7	84	53.0
Leucocytic infiltration	1	1	24	14.0	15	9.4
Islets of Langerhans						
Total involved	9	9	35	20.6	17	10.6
Hyalinized	2		6		6	
Decreased cellularity	7		29		11	
No. with clinical diabetes mellitus	0	*0.0	10	*28.5	2	*11.7

*Expressed as a percentage of the total number of islets involved.

MacDonald and Mallory (1960) found that 60 per cent of cases with portal cirrhosis had significant degrees of pancreatic fibrosis. There are errors involved in a study of this kind, because of the subjective element in the evaluation of pancreatic fibrosis. Woldman, Fishman and Segal (1959) found that in 222 cases of cirrhosis or fatty infilration of the liver, 70 per cent had pancreatic fibrosis. The increased incidence of pancreatitis in patients with cirrhosis of the liver has been attributed to acute episodes of alcohol intake, intermittent lack of protein intake, and to passive venous congestion, resulting from portal hypertension in

cases of liver cirrhosis. In the present study, no definite association between hyalinization and decreased cellularity of the islets of Langerhans and diabetes mellitus was found.

Iron deposition in the liver and pancreas

There was haemosiderin deposition in the liver of 30 per cent of the 329 patients with liver cirrhosis, whereas only 5 per cent of the 100 control patients with extrahepatic disease showed haemosiderin. The haemosiderin deposits also appeared to be greater in amount in the patients with liver disease than in the patients with extrahepatic disease. Of the 329 cases of liver cirrhosis, 3.6 per cent showed an excess of iron in the liver cells, internodular fibrous tissue and Kupffer cells, which was indistinguishable from the livers of patients with idiopathic haemochromatosis. Of the 329 patient with liver cirrhosis, 5.4 per cent showed excess iron in the pancreas, present as granules in the acinar cells and connective tissue.

Causes of Death

Although many factors played a role in causing death in each patient, an attempt was made to estimate from the observations at autopsy the most important cause in each case. The chief causes of death are shown in Table VII. The most

Table VII

Most important causes of death in micronodular cirrhosis and macronodular cirrhosis.

Causes of death	*Types of cirrhosis*			
	Micronodular (170 *cases*)		*Macronodular* (168 *cases*)	
	No. of cases	*Per cent*	*No. of cases*	*Per cent*
Hepatic insufficiency	37	21.8	65	38.7
Associated liver carcinoma	12	7.1	37	22.0
Haemorrhage—total	30	17.6	59	35.1
From varices	26	15.3	55	32.7
From peptic ulcer	4		4	
Cardiovascular Disease—total	24	14.1	7	4.1
Hypertensive, rheumatic, bacterial endocarditis	16		3	
Myocardial infarct	8		4	
Pulmonary infection	20	11.9	6	3.5
Abdominal catastrophies—perforations, strangulation, etc	16	9.4	5	2.9
Non-hepatic malignant tumours	14	8.2	8	4.7

frequent causes of death in micronodular cirrhosis and macronodular cirrhosis were hepatic insufficiency and haemorrhage from bleeding oesophageal varices. In macronodular cirrhosis, 38.7 per cent of the patients died from hepatic insufficiency, and 35.1 per cent from haemorrhage. This was seen to a lesser extent in micronodular cirrhosis where 21.8 per cent of patients died from liver insufficiency and

17.6 per cent from gastro-intestinal haemorrhage. Death from cardiovascular disease was observed more frequently in micronodular cirrhosis than in macronodular cirrhosis.

Discussion

Baggenstoss and Stauffer (1952) in their study of cirrhosis of the liver following viral hepatitis found that cases of post-hepatitic cirrhosis could present either as a nodular or granular liver as in macronodular cirrhosis and micronodular cirrhosis. They suggested that the liver may react in a variety of ways to an attack of viral hepatitis. Sheldon and James (1948) and Kunkel and Labby (1950) found that postnecrotic cirrhosis comprised the common type of cirrhosis of the liver produced by viral hepatitis. Baggenstoss and Stauffer (1952) proposed that the broad zones of atrophy in this group were probably expressive of a severe attack of viral hepatitis and the lack of regeneration. The large regenerative nodules characteristic of postnecrotic cirrhosis were probably evidence of extremely vigorous regeneration after the attack of hepatitis. Neefe and others (1955) in their study examined large numbers of soldiers who had hepatitis during World War II; then re-examined a number of them several years later, and found the frequency of liver cirrhosis was no higher than in a control series. MacDonald and Mallory (1958) believe that the risk of cirrhosis following hepatitis is only 0.7 per cent. Perhaps the most characteristic feature of all was the fact that once cirrhosis was established, the disease was progressive and failed to respond to therapy (Kunkel and Labby 1950). Baggenstoss and Stauffer (1952) found that patients who had posthepatitic cirrhosis died at a mean age of 36 years as compared with a mean age of 50 years for the alcoholic group. In the present study, 4.8 per cent of the patients who died from macronodular cirrhosis were under 20 years of age. Sixty-eight per cent of patients with macronodular cirrhosis and 40.4 per cent with micronodular cirrhosis were diagnosed before autopsy. A higher rate of clinical diagnosis was obtained in macronodular cirrhosis due to the greater degree of hepatocellular damage. An increased incidence (11.7 per cent) of diabetes mellitus was also found in patients with micronodular cirrhosis, compared with the incidence (2.6 per cent) in the patients autopsied at this institute.

It appears that the relationship between infectious hepatitis and liver cirrhosis is obscure. Hällén and Krook (1963) found the liver to be coarsely nodular in 36 per cent of cases with posthepatitic cirrhosis, 4 per cent with alcoholic cirrhosis and in 26 per cent of cases of cryptogenic cirrhosis. Dible (1951) and Perkins et al (1950) also found that hepatitis may produce the morphological equivalent of portal cirrhosis or postnecrotic cirrhosis.

The hepatic changes in the alcoholic have been related to nutrition as chronic alcoholics usually eat sparingly and erratically. It has been claimed that lack of lipotropes like choline or methionine cause fat infiltration of the liver, which leads to a portal-type of micronodular cirrhosis. Kimmelstiel, Large and Verner (1952) have shown that alcohol has an effect upon fat metabolism independent of nutritional factors. Thus it seems that alcohol may have direct and indirect effects on hepatic fat metabolism quite independently of nutritional changes. The alcoholic

commonly presents with micronodular, portal cirrhosis, but postnecrotic cirrhosis with a macronodular pattern is also seen (Baggenstoss and Stauffer, 1952). In the present study, a history of excess alcohol intake was noted in 20 per cent of cases with micronodular cirrhosis and 11.9 per cent of cases with macronodular cirrhosis. A history of jaundice or hepatitis was noted in 14.2 per cent of patients with macronodular cirrhosis and in only 3.5 per cent with micronodular cirrhosis.

The patients who had macronodular cirrhosis died at a younger age than patients with micronodular cirrhosis. The average age at death in cases with macronodular cirrohosis was 58 years, and in patients with micronodular cirrhosis 62 years. Baggenstoss and Stauffer (1952) noted after an attack of hepatitis cirrhosis can apparently develop in a relatively short time, even in a matter of weeks. Sherlock (1948) noted the rapidity with which cirrhosis may develop in these patients.

The average weight of the livers in patients with micronodular cirrhosis was much heavier by 400g than in cases with macronodular cirrhosis. Connor (1939) and Hall and Morgan (1939) found the livers in general to be smaller than normal in alcoholic cirrhosis. Fat infiltration was observed more commonly and was more severe in micronodular cirrhosis than in macronodular cirrhosis. There was a heavier lymphocytic infiltration of the fibrous tissue and liver parenchyma in macronodular cirrhosis than in micronodular cirrhosis. In accordance with the findings in the present study, MacSween and Jackson (1966) observed that the commonest cause of death in micronodular cirrhosis and macronodular cirrhosis was hepatic failure. Here 38.7 per cent with macronodular cirrhosis and 21.8 per cent with micronodular cirrhosis died of liver failure. There was an associated primary liver cell carcinoma in many of these patients. A primary hepatocellular carcinoma of the liver was found in 22 per cent with macronodular cirrhosis and in 7 per cent with micronodular cirrhosis. Death from bleeding oesophagael varices was more frequent in patients with macronodular cirrhosis than in micronodular cirrhosis. This suggests that portal hypertension is more severe, and is present more often in macronodular cirrhosis than in micronodular cirrhosis. This is contrary to the findings of Baggenstoss and Stauffer (1952) who found that in alcoholic cirrhosis the regenerative nodules were smaller and more numerous and consequently compressed a greater number of smaller hepatic and portal venules, thus causing a higher incidence of portal hypertension.

Demonstrable haemosiderin pigment was observed in a large proportion of livers from patients with liver cirrhosis, both micronodular and macronodular types. In the control patients without hepatic disease, haemosiderin in the liver was significantly less frequent (5 per cent) and slight in quantity. Thirty per cent of the 329 patients with micronodular cirrhosis and macronodular cirrhosis had haemosiderin in the liver cells, but only 3.6 per cent of the livers contained iron to the same extent as in cases with haemochromatosis. In approximately 60 per cent of these there was a history of multiple blood transfusions, excess alcohol and iron intake to explain the presence of hepatic haemosiderin. Pancreatic siderosis was found in 5.4 per cent of the 329 patients with liver cirrhosis, but the iron deposition was light and not as heavy as in haemochromatosis. There is some degree of overlap between siderosis in liver cirrhosis and haemochromatosis. Thus, cases of liver cirrhosis and haemosiderosis should be classified as pigment

cirrhosis, unless there is a strong genetic evidence for idiopathic haemochromatosis.

The correlation between aetiological factors and postmortem changes is poor, and the further study of morphological features would be of most value in the early stages of the disease. It would appear that a satisfactory classification of liver cirrhosis would be an aetiological one with a morphological description of the pathological features.

Summary

During 1938 to 1966 inclusive, 22,050 autopsies were performed by the Staff of the Institute of Pathology, Belfast. The incidence of liver cirrhosis (640 cases) found at autopsy was 2.9 per cent. There were 170 patients with micronodular cirrhosis and 168 with macronodular (postnecrotic/posthepatitic) cirrhosis. These groups of patients were studied and compared clinically and pathologically. Patients with macronodular cirrhosis died at a younger age than those with micronodular cirrhosis. Approximately 4.8 per cent of the patients with macronodular cirrhosis died before the age of 20 years. There was no sex difference in micronodular cirrhosis and macronodular cirrhosis.

Jaundice and ascites were more frequent in macronodular cirrhosis. Hepatic insufficiency and haemorrhage from oesophageal varices were the most common causes of death in both types of liver cirrhosis. Portal hypertension, as evidenced by ascites, splenomegaly and oesophageal varices was more common in macronodular cirrhosis than in micronodular cirrhosis. The average weight of the liver in micronodular cirrhosis was 400g heavier than in macronodular cirrhosis. The incidence of primary hepatic carcinoma was 22 per cent in macronodular cirrhosis and 7 per cent in micronodular cirrhosis. Portal vein thrombosis was associated with the hepatic carcinoma. Peptic ulcer was found in 15.2 per cent with micronodular cirrhosis, 6.5 per cent with macronodular cirrhosis and in 3.7 per cent with extrahepatic disease. Diabetes mellitus was observed in 11.7 per cent with micronodular cirrhosis, 2.9 per cent with macronodular cirrhosis and in 2.6 per cent of cases with extrahepatic diseases. Approximately 50 per cent of patients with micronodular cirrhosis were not diagnosed until autopsy. Sixty-eight per cent of patients with macronodular cirrhosis were diagnosed before autopsy, presumably because of the greater degree of liver parenchymal damage.

Haemosiderin pigment was present in 30 per cent of the 329 patients with micronodular cirrhosis and macronodular cirrhosis, but only 3.6 per cent of the livers contained iron to the same extent as in patients with haemochromatosis. There was a poor correlation between the aetiological factors and postmortem changes. A satisfactory classification of liver cirrhosis would be an aetiological one with an anatomical or pathological description.

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